ARCHIVES OF PEDIATRICS

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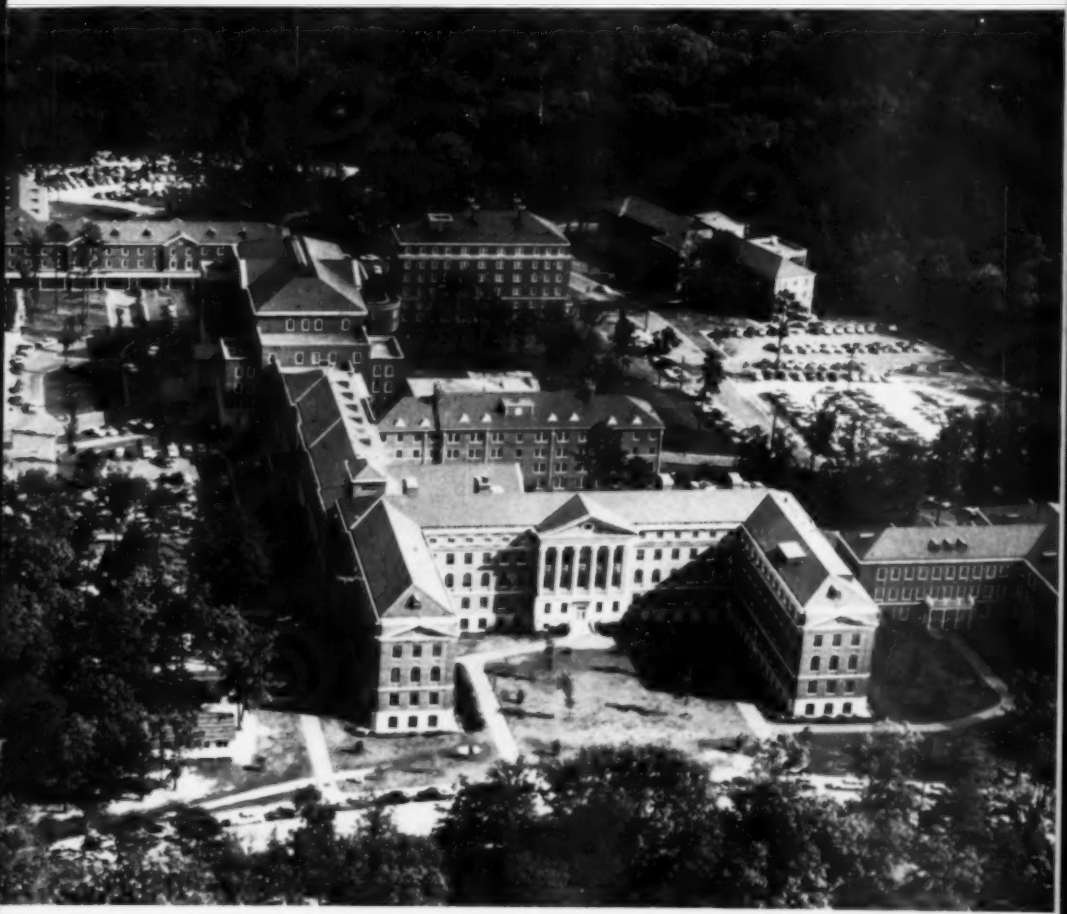

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The Cover . . .

The broad vista of the University of North Carolina Division of Health Affairs at Chapel Hill pictured on this month's front cover, includes the UNC Schools of Medicine, Dentistry, Nursing, Public Health and North Carolina Memorial Hospital.

on the pathogenesis of pyelonephritis:

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References: 1. Schreiner, G. E.: A.M.A. Arch. Int. M. **102**:32, 1958. 2. Freedman, L. R., and Beeson P. B.: Yale J. Biol. & Med. **30**:406, 1958. 3. Rocha, H., et al.: Yale J. Biol. & Med. **30**:341, 1958.

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1. Kaessler, H. W.: Arch. Ped. 74:47 (Feb.) 1957.
2. Kahan, H. *et al.*: Arch. Ped. 73:125 (Apr.) 1956.
3. Editorial: J.A.M.A. 165:254 (Sept. 21) 1957.

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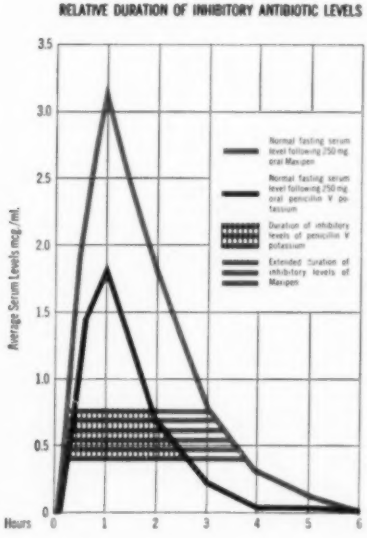

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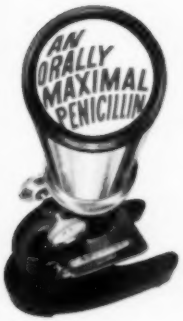

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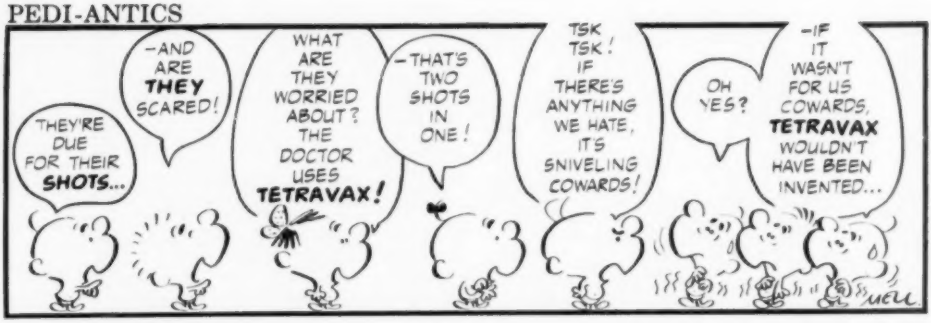
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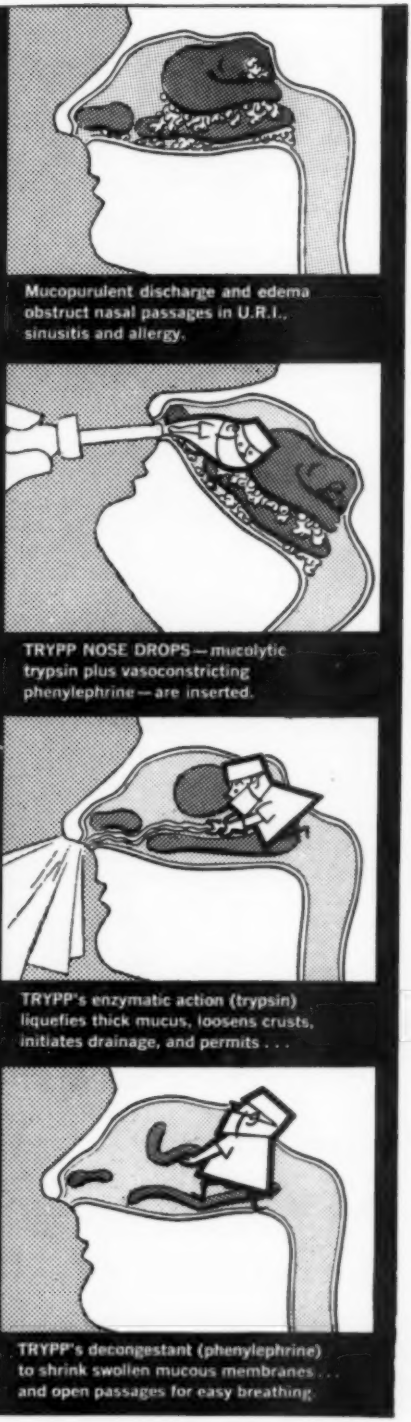
2. Taterka, H. and Wasserman, E.: personal communciation.



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News and Notes . . .

The Bronx Pediatric Society will meet on Wednesday, December 14, 1960 at 8:30 P.M. at the Morrisania Hospital, Bronx, N. Y. Dr. Edmund P. Fowler of the College of Physicians, Columbia University, will present the James Harkins Memorial Lecture, Problems in Pediatric Otology. Officers of the Society for 1960-61 are Doctors Arthur Goldfarb, president; Louis Penn, vice-president; David L. Milliken, secretary-treasurer.

The American Association of Poison Control Centers' third annual meeting will be held on October 18th at the Palmer House, Chicago. For further information, write: Harry C. Shirkey, M.D., The Children's Hospital, 712 South 30th St., Birmingham, Alabama.

Publisher's Note . . . This year's front cover presentation of many outstanding Medical Centers is bringing **Archives of Pediatrics** interested expressions from subscribers and readers. Apparently recognizing his Alma Mater, a doctor from Cali, Colombia, offered to pay for a copy of a cover photograph. We happily sent it to him with our compliments! We will be glad to hear from you.

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Pectus Carinatum, Pigeon Breast and Related Deformities of the Sternum and Costal Cartilages

CHARLES W. LESTER, M.D.*
New York

Pigeon breast, chicken breast, pyramid chest and similar protrusion deformities of the sternum, and the protrusion deformities lateral to the sternum and in the costal arch, involving the costochondral junctions, are frequently ascribed to rickets although they have no relation whatever to that disease. Actually they are of a developmental nature and should be classified with congenital deformities.

The deformities are of several types. Two are in the midline with the sternum the most prominent part; two are lateral to the sternum with the costochondral junctions the most prominent part; and there may be various combinations of these.

Because the deformities are varied the terminology is also varied and therefore inexact and confusing. Hence, in this presentation *pectus carinatum*, which means *keel chest*, will be employed and further modified to indicate site or type.

In one type of midline deformity the sternum protrudes in an arcuate fashion and the upper or midportion of the sternum is most prominent. (Fig. 1). In the other, the sternum protrudes obliquely and the xiphoid is the most prominent portion. (Fig. 2). In either case the costal cartilages must curve forward to meet the sternum and those cartilages attaching to the sternum where it protrudes most will have the maximum deformity. With the arcuate type of protrusion there may be a transverse groove similar to that of funnel chest. With the oblique type an apparent depression is present lateral to the lower end of the sternum due to the forward curve of the costal cartilages.

* *From the Chest Deformity Clinic, Hospital for Special Surgery, New York, N. Y.*

In one type of the lateral pectus carinatum the protrusion corresponds to the costochondral junction and the involved costal cartilages point back to meet the sternum. (Fig. 3). In the other type the costal arch flares and when this is bilateral the deformity can be confused with funnel chest. (Fig. 4). The higher deformities are usually unilateral but if they are bilateral the protrusions are at different levels.

Fig. 1-A. Arcuate type of pectus carinatum in boy, age 9.

Fig. 1-B. Lateral roentgenogram. Note apparent end of ribs posterior to sternum.

Combinations of these types may be present in the same patient. More often, however, pectus carinatum may be combined with the features of funnel chest (pectus excavatum). Not infrequently an arcuate pectus carinatum is mistaken for funnel chest but the differentiation is easily made by measuring the movement of the xiphoid during respiration. In a child with funnel chest the xiphoid retracts during inspiration, or may be stationary if the child is older, while with pectus carinatum the xiphoid moves forward with the costal arch.

The lateral roentgenogram of a midline pectus carinatum is characteristic. The cartilages protrude forward to meet the sternum and, since they are not opaque to the x-rays, the ribs seem to terminate in a plane behind the sternum and not at the sternum as in the usual lateral chest film.

Fig. 2-A. Oblique type of pectus carinatum in boy, age 15.

Fig. 2-B. Lateral roentgenogram.

If the incidence of pectus carinatum could be determined it would probably be found about equal to that of funnel chest. However, the deformities and the symptoms of pectus carinatum are seldom as pronounced as those of funnel chest and fewer of the former seek medical advice, thus making pectus carinatum seem less common.

The etiology and pathogenesis have been discussed in previous papers[1,2] and will be considered here in less detail.

It should be noted that the same etiological factors appear in funnel chest as in pectus carinatum but in different proportions. In arachnodactyly (Marfan's syndrome) the chest deformity, when present, may be either pectus carinatum or funnel chest. (Fig. 4).

Heredity is an important factor and it is common to both the protrusion and depression deformities. Furthermore, a forebear with funnel chest may be responsible for a descendant with pectus carinatum and vice versa. In some instances the hereditary factor is easily recognized and may be present in three or four generations. Usually the hereditary factor is recessive and it is necessary to investigate relatives in collateral lines, such as cousins or uncles, for similar deformities which suggest a common ancestor with the deformity. In many instances no similar deformity can be found but this does not prove that one did not exist.

Fig. 3. Lateral pectus carinatum in boy, age 8, who also has torticollis.

Fig. 4. Girl, age 4, with costal arch protrusion. This has the appearance of funnel chest but during inspiration the xiphoid moves forward in a normal manner indicating a protrusion deformity. The child has multiple deformities associated with Marfan's syndrome.

Both pectus carinatum and pectus excavatum have diaphragmatic action and disproportionate rib growth in their pathogenesis. In pectus carinatum the disproportionate rib growth is the major element. If pairs of ribs attached to the sternum grow propor-

tionately longer than the ribs above and below, the sternum will be pushed forward where the ribs attach and the costal cartilages will incline forward from the costochondral junctions. If this is in the midportion of the sternum, the sternum will protrude in an arcuate fashion. If it occurs at the lower end of the sternum, the sternum will protrude in an oblique fashion. If it occurs in the costal arch the costal arch will flare.

If disproportionate rib growth occurs only on one side the sternum will not be protruded but the ribs will buckle forward at the costochondral junction and the protrusion will be lateral to the sternum. If this unilateral overgrowth occurs in a rib of the costal arch the arch will flare on that side.

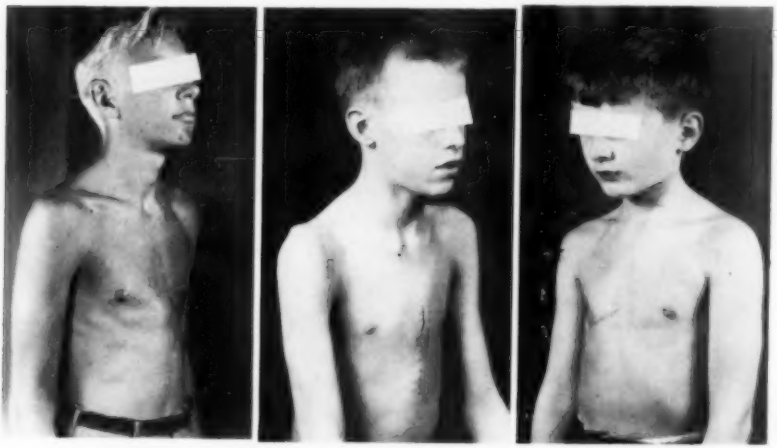

Fig. 5 A. Patient in Figure 1 after operation.

Fig. 5 B. Patient in Figure 2 after operation.

Fig. 5 C. Patient in Figure 3 after operation. The torticollis has also been corrected.

The diaphragmatic pull has a minor role in pectus carinatum. If the diaphragm does not enlarge to keep pace with the protruding ribs it may increase the funnel chest appearance of the arcuate pectus carinatum. The chief effect of this disproportion, however, is not on the appearance but on the symptoms.

The symptoms of pectus carinatum, when present, are not as severe nor as frequent as those of pectus excavatum but they do fall in the same categories of respiratory and cardiac disabilities. Although the symptoms are essentially the same the mechanisms are quite different.

The respiratory symptoms in pectus carinatum are those of ineffectual cough. This is probably brought about by limited excursion of the diaphragm which has been stretched by the chest deformity and not by a deformity of the diaphragm such as appears in funnel chest. Because the bronchial secretions cannot be expelled a mild bronchitis becomes chronic or progresses to pneumonitis. Chronic cough and repeated acute respiratory infections certainly disappear when the deformity is corrected.

Decreased exercise tolerance and functional heart murmur are not so easily explained. The best explanation of these is that because the protruding sternum increases the precordial space, the heart is allowed to rotate enough during systole to constrict the outflow tract by torsion. This decreases the flow of blood to the lungs and to the periphery at a time when it should be increased. It can also account for a functional murmur. These symptoms disappear, sometimes dramatically, after the deformity is corrected.

The psychological effect of the deformity is usually present and frequently severe. Whether male or female, a well-formed thorax is greatly to be desired and a deformed thorax produces distress out of all proportion to the deformity. It should also be noted that a pectus carinatum prominent enough to cause embarrassment usually produces physical symptoms as well which may not be recognized until the deformity is corrected.

The treatment of pectus carinatum is surgical. Because growth is a factor in producing the deformity operation on the midline deformities may be deferred until the sternum approaches its maximum growth, although the operation can be done at any age. The lateral pectus carinatum may be operated upon earlier. The operations are in the nature of thoracoplasty, i.e. the deformed bone and cartilage are resected leaving the periosteum and perichon-

drium which drop to a normal position permitting the structures to regenerate in their normal positions.

In the midline deformities, whether arcuate or oblique, the third to the seventh inclusive costal cartilages are resected subperichondrially to the extent of their deformity, which, incidentally, is more than it appears to be. The gladiolus of the sternum is then stripped of its periosteum and removed from a point below its junction with the manubrium down to the xiphoid, which is retained. The wound is then closed in a manner to maintain a correct position.

If the operation is undertaken before the sternum has attained an adequate growth the second sternal segment is removed subperiosteally, leaving its cartilaginous ends. If this does not allow correction of the position another segment may be similarly removed. The remainder of the operation is unchanged.

When the deformity is lateral to the sternum the involved ribs and costal cartilages are resected subperiosteally and subperichondrially to the extent of their deformity and allowed to drop into place.

These operations may seem radical but in 45 operations there has been no fatality and only a few minor complications. The patients are confined to the hospital for about a week. The results, both physical and psychologic have been good (Fig. 5) but, naturally, the more recent operations have been cosmetically better than the early ones performed while the procedure was being developed.

SUMMARY

Pectus carinatum is a protrusion deformity of the sternum and costal cartilages developing with growth.

It may be in the midline or lateral to the sternum or in the costal arch. Symptoms can be both physical and psychologic. The treatment is surgical and the results are good.

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Malignant Lymphoma in Childhood

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The term malignant lymphoma was introduced in 1942 by Gall and Mallory[1] to include a group of maladies characterized by progressive tumor-like formation of the lymphatic system. The neoplastic nature of the diseases described under this term is generally agreed upon, although as Robb Smith[2,3] has stated "The distinction between blastomatoid conditions and true blastomata is more difficult in lymphoreticular tissue than in any other tissue".

Various classifications of malignant lymphoma have been put forward[4,5,6,7,8]. The classification of Parker et al[9] is the most practical since it demonstrates the origin and fate of the various lymphomas. Their classification is based on the embryological and histological structure of the lymph node.

The lymph node arises in the third fetal month from a focal thickening of the mesenchyme along lymphatic channels[10,11,12,13]. Histologically the lymph node is composed of the following structures:

(a) Lymph sinuses derived embryologically as outgrowths in lymphoid tissue from the original lymph channels and surrounded by medullary cords composed of lymphocytes, reticulum cells, fibroblasts and plasma cells.

(b) Follicles: formed of lymphocytes, lymphoblasts and some reticulum cells derived probably from the littoral cells lining the primitive lymphatic sinuses.

(c) Reticular tissue distributed throughout the rest of the cortex and medulla and derived from the early connective tissue cells.[14]

Parker et al [9] classified malignant lymphoma according to the cell of origin of the tumor into tumors arising from lymphocytes,

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lymphoblasts, histiocytes, reticulum cells or plasmocytes. As is evident from their classification (Table 1) all malignant lymphomas might ultimately terminate in leukemia of one type or the other.

TABLE I

CLASSIFICATION OF MALIGNANT LYMPHOMA

Modified after Parker et al[9]

Proliferating cell	Lymphoma	Leukemia
Lymphocyte	Lymphocytoma	Chronic Lymphatic
	Lymphosarcoma	Acute or chronic lymphatic
Lymphoblast	Lymphoblastoma	Acute lymphatic
	Giant follicular lymphoma.	Acute or chronic lymphatic
Reticulum cell	Reticulum cell sarcoma	Histiocytic
	Hodgkin's (paragranuloma, granuloma, sarcoma).	
Plasma cell	Plasmocytoma	Plasma cell
	? Myelomatosis	

In spite of the vast literature on the subject in adults there are relatively few references on the incidence and course of malignant lymphoma in children. Malignant lymphoma is not a rare form of malignancy in the pediatric age group. In a series of *273* cases of malignant disease in children, *28* cases were due to tumors of the lymphatic system.[15] Custer[16] in 1954 collected *27* cases of lymphosarcoma (excluding leukemia) out of 583 children with malignant diseases admitted to the Cancer Memorial Hospital. Only 5 cases were encountered in children below 5 years old, the remaining *22* cases affected older children from 5 to 15 years. Isolated cases of malignant lymphoma in children were also reported by Baggenstoss[17], Hashim and Diwani[18] and others.

In this article we are going to present *3* cases of malignant

lymphoma in children with unusual features: a case of giant follicular lymphoma and 2 cases of reticulum cell sarcoma.

1. *Giant Follicular Lymphoma*:

The condition was probably first described by Becker in 1901.[19] Other cases were later reported by Foix,[20] Kettle[21] & Young.[22] The full clinical picture of the disease, however, was first described by Brill & Symmers. The disease is commonly known by their name.[23, 24] Other names for the condition are follicular lymphoblastoma, giant follicular lymphodenopathy, giant lymph follicle hyperplasia.

Follicular lymphoma is a relatively rare condition. Baggenestoss[17] collected 72 cases from the literature up to 1940. The disease affects middle age and the elderly with a peak incidence at 50-60 years.[25] Males are more commonly affected than females.[26] It affects mainly cervical and inguinal lymph nodes[27]; the affected nodes enlarge slowly and further groups become affected. The lymph nodes sometimes reach a huge size; they are discrete rounded, rubbery and not fixed. Splenomegaly is common, but hepatomegaly is not so frequent. Involvement of the lacrimal glands and exophthalmos were described as characteristic features.

Giant follicular lymphoblastoma is the most benign form of malignant lymphoma with a long course sometimes up to 20 years.[28,13]. Brill[23] & Symmers[24] considered the disease as a hyperplastic proliferation of the lymph nodes. Later Symmers[20] and Beahr et al[30] revised their views and considered the condition neoplastic in origin and potentially malignant. There is now little question as to the individuality or ultimate malignancy of the condition.[25,31] After a long steady course some cases may pass into lymphocytoma, lymphoblastoma, lymphosarcoma, reticulum cell sarcoma or Hodgkin's disease with or without leukemic states.[13] The disease is usually sensitive to radiotherapy, although recurrence is the rule. Over 60% of cases survive five years after treatment.[26]

Pathologically the follicular pattern of the node can be seen by the naked eye on the cut surface as masses of cream colored nodules almost 1 mm. in diameter. Histologically there is proliferation of lymphoblasts and reticulum cells within the lymphoid follicles,[32, 22] producing an increase both in number and size of the individual follicles. In advanced cases transitional stages between

follicular lymphoma and other more malignant conditions may be seen. The histological diagnosis of the condition is often difficult since it may resemble secondary follicular hyperplasia of the lymph node.

CASE ONE

First admission: G. M. a boy aged 2½ years was first admitted to the hospital in April 1955 with the chief complaint of swelling of the neck. The swelling was noticed one month before admission and has been progressively enlarging since then. The past history and family history were not remarkable.

Fig. 1. Case 1, May 1955.

Examination revealed a well nourished child with bilateral markedly swollen elastic, discrete and painless cervical and submandibular glands. Axillary and inguinal glands were slightly enlarged. Both the liver and the spleen were felt 3 fingers below the costal margin. Physical examination was otherwise negative. (Fig. 1)

INVESTIGATIONS

Hb.: 70%—R.B.Cs. 4,200,000—Total W.B.Cs. 14,200—
Polymorphs 63—Lymphocytes 33—Monocytes 5—
Normal platelets in film.
Bone marrow: cellular, myeloid: erythroid ratio 1.5 : 1 with a normal differential count: myeloblasts 6—myelocytes 6—
Juvenile 13—Staff 15—Segmented 17—Lymphocytes 2, Baso-

phil 1, Eosinophil 0, Normoblast 35, Macroblasts 5.

Tuberculin Test: Negative.

Radiological examination of the chest, skull and long bones was negative.

Urine and stools were free.

Progress: During his stay in the hospital both the cervical and axillary glands progressively enlarged. Edema of the face and of the forearms developed probably from pressure by the glands on the draining lymphatics. One of the neck glands was excised for biopsy and the following pathological report was made: "The lymph node is grossly enlarged. Microscopic examination showed that the capsule is intact and revealed the presence of numerous large follicles uniformly scattered throughout the cortex and medulla of the lymph node which are crowded against each other. The follicular structures are mainly composed of reticulum cells with a narrow ring of lymphocytes. The surrounding lymphoid structure is obviously compressed by the expanding newly formed follicles and in some places a crack separates the two structures. Diagnosis: giant follicular lymphoma." (Fig. 2)

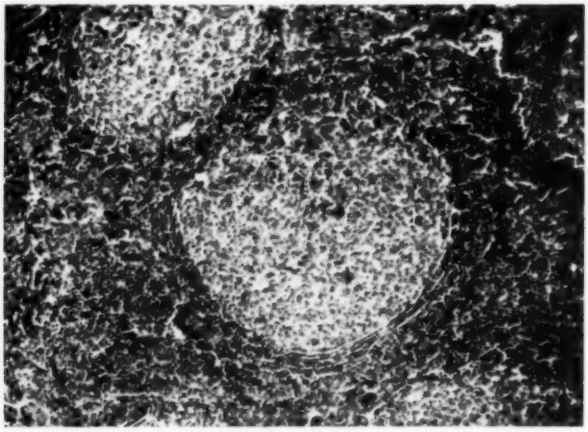


Fig. 2, Case 1 Giant Follicular Lymphoma

The child was discharged at the mother's request a month after admission.

Second admission: He was readmitted in October 1955 because of the development of bilateral proptosis and ptosis of the left eye,

which the mother noticed one month previously. The edema of face and upper limbs had disappeared by this time and his general condition had improved but the glandular enlargement persisted. Exophthalmus of both eyes was evident with ptosis of left eye. Ophthalmic examination revealed sluggish reaction of right pupil which was more dilated than normal, while the left pupil was widely dilated and fixed. Fundi showed blurring of margin and some congestion of veins, a picture of early papilledema. Investigations done on the second admission were essentially similar to the previous investigations. X-ray of skull was negative.

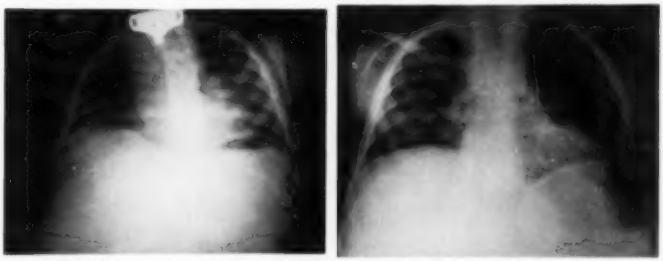


Fig. 3, case 1, Enlarged Mediastinal Glands (Tracheotomy).
Fig. 4, case 1, Shrinkage of Mediastinal Glands.

Progress: The child remained in the hospital for 2 months, on tonics only. During this time the proptosis has markedly regressed and pupillary reactions became active. He was discharged with minimal proptosis and slight ptosis of left eye.

Third admission: He was readmitted for the third time in October 1955 because of development of severe stridor and cyanosis. The mother stated that after the second discharge from the hospital his general condition improved and he started to put on weight. On the night of admission he developed severe dyspnea with labored breathing. Examination revealed a distressed blue child with marked inspiratory stridor and retraction of subcostal margin. Chest was free apart from upper respiratory sounds heard on auscultation. Eyes looked the same; skull circumference was 48 cm.; liver was 5 fingers below costal margin and the spleen was three fingers enlarged. The neck and axillary glands were much more swollen than before. Mouth and throat were free and laryngoscopy revealed normal findings. Tracheotomy was done two hours after admission with marked relief of the respiratory difficulty. Investi-

gations done on the third admission were essentially negative except for a moderate degree of anemia (Hemoglobin 60%) and marked enlargement of the mediastinal glands was evident radiologically (Fig. 3).

Because of technical difficulties the child did not receive deep x-ray therapy. In spite of this the mediastinal shadows gradually decreased in size (Fig. 4), the respiratory difficulty disappearing altogether in 3 months time. The tracheotomy tube was ultimately removed and the child was discharged in February 1957.

The child has been seen sporadically ever since and is still living (March 1959); the mother refusing any medication. During the last year the general condition of the child has deteriorated with

Fig 5, Case 1, March 1959.

Fig. 6, Case 2.

Fig. 7, Case 2, Note nodules on Scrotum.

emaciation and easy fatigability. The liver has progressively enlarged in size now reaching almost 8 fingers below the costal margin. The neck glands, however, surprisingly have regressed in size. (Fig. 5)*

COMMENT

This case demonstrates the relatively benign course of follicular lymphoblastoma. The child was still living almost four years after the onset although no specific treatment was received.

The exophthalmos which developed in our case was associated with early papilledema, ophthalmoplegia and ptosis. There was no evidence of involvement of the C. N. S. In fact involvement of the nervous system is extremely rare in follicular lymphoblastoma.[9] Baggenstoss[17] attributed the exophthalmos in this condition to involvement of lacrimal glands; the lacrimal glands of our patient were normal. The exophthalmos and the other ocular changes are most probably due to retroorbital deposits.

The most striking feature of this case is the fluctuating course of the disease with spontaneous remissions and exacerbations; the cervical gland enlargement disappeared about 4 years after the onset of the illness, the exophthalmos disappeared spontaneously 3 months after its appearance and the mediastinal glands shrunk in size without treatment in 3 months time. We could not find in the available literature any reference to a fluctuating course in giant follicular lymphoma. The disease is usually decribed as having a slow but steady course.[39]

2. *Reticulum cell sarcoma:*

As early as 1913 Ewing suggested the possibility of a tumor arising from the reticulum cells of lymph nodes. The term reticulum cell sarcoma (Retothelsarcam) was first introduced by Roulet in 1930.[33,34] The reticulum cell sarcoma is a lymphoma composed purely of reticulum cells. The reticulum cell has an origin and function similar to the wandering histiocyte, plasmatocyte, macrophage and wandering mononuclear cells. The cell is derived from mesenchyme and appears in embryonic life at almost the same time as the fibroblast.

The tumor should not be classified as a lymphosarcoma. The main differences are: 1 — the reticulum cell is different embryologically from the lymphocyte, reticulosarcomata never ending in lymphatic leukemia as do some lymphosarcomata, 2 — reticulosarcomata may arise primarily in bone while lymphosarcomata do not, 3 — the age

*Since this article was written the child died at home in April 1959 following a convulsive fit which lasted 24 hours.

incidence is different; lymphosarcomata affecting younger age groups.

Since reticulum cells are distributed all over the body the neoplasm may arise in any tissue. The commonest sites however are the lymph nodes, liver, spleen, kidneys, lungs, bones (Ewing tumor) and C. N. S. (from microglia). Almost every other organ has been described as being involved.[35,36,37] Owing to the widespread nature of the tumor it is often difficult to state if the various deposits are multiple primaries or metastases from a primary focus. Widespread metastases through lymphatics and blood stream however are sure to occur. The tumor is usually predominant in patients in the older age group (excluding Ewing's tumor of bone), it is commoner in males in the ratio of 2:1. Histologically reticulum cell sarcoma is classified into 2 types[1]: those composed of relatively well differentiated wandering cells with phagocytic properties resembling the monocytes or clasmatocyts (clasmatocytic type) and those made up of highly undifferentiated presumably pleuripotential cells (stem cell type). Previously Robb Smith[2] classified the reticulosarcomata into undifferentiated and differentiated types. He classified the latter type according to the fiber forming potentialities of the mother cell into histoid, hemic and mixed types. These subdivisions are however of minor clinical importance since all types of reticulosarcoma have an ultimately bad prognosis [38] The average duration of life was given as 1 to 2 years. The tumor is extremely radiosensitive and is often sensitive to nitrogen mustard.

CASE TWO

First admission: A. A., male aged 9 years was admitted to the Children's Hospital for the first time on September 3rd, 1956 complaining of marked exhaustion, easy fatigability and swelling of both sides of the neck. The child was admitted 15 days before to a fever hospital where he received glucose injections and was discharged without a definite diagnosis.

Examination revealed a feverish, pale, thin and toxic child. Bilaterally enlarged upper cervical glands were felt. They were firm, discrete, about 3 x 3 cm. in size with no breaking down. Axillary and inguinal glands were less markedly enlarged. The spleen was 3 fingers below the costal margin, the liver was moderately enlarged and soft. Hemorrhagic spots were scattered all over the trunk and there were areas of subcutaneous ecchymosis. There

was no evidence of other tumor masses. Two huge abscesses in the thighs were present presumably as a complication of the hypodermoclysis which he received before. The rest of physical examination revealed normal findings.

INVESTIGATIONS

Blood picture: Hb. 32%—R.B.Cs. 1,640,000—W.B.Cs. 3200
Polymorphs 62%—Lymphocytes 30%—Monocytes 4%—
Eosinophiles 4%—No abnormal cells. Platelets 167,000.
Bleeding time 3 minutes. Coagulation time 3.5 minutes.
E.S.R. 88 min.
Blood cholesterol 230 mgm. %.
Tuberculin: negative.
Stools & Urine free.

Sternal puncture: normal myelogram: marrow hypercellular. Myeloid: erythroid ratio (1.5 : 1)—*Diff. count:* Basophil 1—Eosinophils 4—Myelocytes 10—Juveniles 10—Staffs 16—Segmented 20—Lymphs 24—Macroblasts 3—Normoblasts 35.

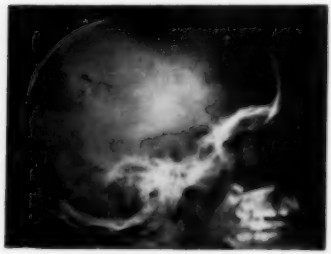
Blood proteins 6.5 gm. %. Liver function tests showed slight impairment of liver function.

Progress: Child remained febrile for the first week, temperature varying between 27-39 C. He received antibiotics and the abscesses were incised and drained. The glands regressed in size and the petechiae disappeared 2 weeks after admission. The anemia and the general condition improved. The parents insisted on discharging the child 2 weeks after admission.

Second admission: The child was not seen except two months after discharge on 25.11.56 when he presented with bilateral scrotal swelling which had been noticed a week before. Examination revealed a pale child with generalized enlargement of servical, axillary and inguinal glands. The glands were discrete and about 2 x 2 cm. in size. Both the liver and spleen were about 4 fingers enlarged. Multiple cutaneous nodules were found on the head, neck and scrotum. They were painless, firm, indurated, about 1 cm. x 1 cm. in size, and dusky red in color. Both testes were hard and enlarged about 10 x 4 x 4 cm. in size each. Epididymis could not be differentiated from the testes. The scrotal skin was dark red with firm subcutaneous nodules. The rest of the physical examination was not remarkable. (Figs. 5 and 7)

Progress: Four days after admission left facial paralyses was noted.

The facial paralysis improved without specific treatment in a week's time. On 12..12.59, the child was put on nitrogen mustard 15 mgm. every other day for 15 injections with no improvement. The testes progressively enlarged to a remarkable size, new skin nodules appeared, the neck glands enlarged, a swelling appeared in the right zygoma on 23.12.56 and subcutaneous ecchymosis appeared a week later. Deep x-ray treatment was started on 2.2.57 with rapid regression of the size of the glands, testes and facial swelling. Fifteen days later deep x-ray therapy had to be stopped because of severe leukopenia. Swellings increased quickly in size. The child passed into coma on 28.2.57 and died on the next day. An autopsy permission was refused by the parents.



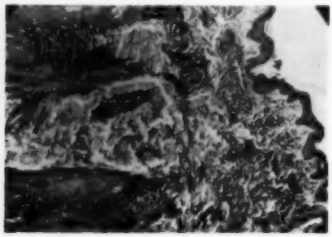


Fig. 8, case 2, Skull defects in Parietal Bone.

Fig. 9, case 2, The dermis is infiltrated with reticulum cells. A dense infiltrate is surrounding a hair follicle.

Investigations on the second admission were essentially similar to previous studies; the myelogram and hemogram were repeatedly normal until 3 days before death. Both fundi were normal. X-ray examination revealed destruction of the right parietal bone with sharp edges (Fig 8). The rest of the skeleton, and urinary tract were free. Three days before death immature cells appeared in the peripheral blood. It was difficult to decide as to the nature of the cells whether they were myeloblasts or histiocytes. This terminal blood count showed: 59% blasts (10% broken down), 24% polymorphs and 12% lymphocytes; total count was 12,000.

Biopsies were taken from a skin nodule and the scrotal swelling. The following are the biopsy reports:

Skin nodule: the dermis and subcutaneous fat are infiltrated by a malignant tumor nodule mainly made of large polygonal cells which have abundant pale cytoplasm and large oval, round or

reniform vesicular nuclei. No giant or multinucleated cells could be seen in sections examined. Reticulin stain revealed abundant argentophil fibers separating the cells from each other. *Diagnosis: reticulum cell sarcoma.* (Fig. 9).

Testis: The testicular tissue is diffusely infiltrated by a reticulum cell sarcoma. Few degenerated seminiferous tubules are seen widely separated from each other by the tumor tissue. (Fig. 10)

COMMENT

This case demonstrates clearly the difficulty of diagnosis of the early stages of reticulum cell sarcoma. The child was originally diagnosed as fever of obscure origin and later had signs and symptoms suggestive of leukemia. During the course of the illness however the widespread dissemination of the tumor in the glands, skull, C.N.S., skin and testes became evident.

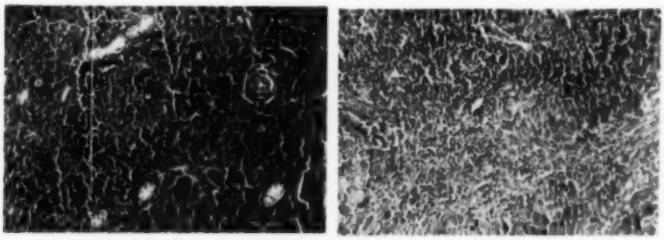


Fig. 10, case 2, Testes infiltrated by reticulum cells.
Fig. 11, case 3, Reticulum Cell Sarcoma of Cervical Lymph Node.

Involvement of the central nervous system in this case was evidenced by the facial paralysis and the terminal coma. Erosion of the parietal bone which was shown radiologically was not apparently associated with gross brain deposits. C.N.S. involvement is reported to occur in 16% of malignant lymphoma and in 33% of reticulum cell sarcoma.[9] Four neurological syndromes may be produced by malignant lymphoma (1) compression of spinal cord. (2) Involvement of cranial nerves commonly V, VI, VII, VIII, IX. (3) Meningeal invasion. (4) Primary cerebral malignant lymphoma.

Involvement of the testes by reticulum cell sarcoma is very rare. In 74 cases of malignant lymphoma only one case of testicular involvement has been described.[1] In fact concomittant bilateral malignant tumors of normally located testes is very rare. Hotchkiss[14] collected 21 cases from the literature, all adults. He pre-

sented a case of reticulum cell sarcoma of both testes in a male aged 59 years; this patient also had generalized glandular enlargement and skin nodules very simlar to those of our case. This combination of skin nodules and testicular tumor was first described by Mallassez in 1877.[39] Since that time several reports of similar nature have appeared.[40,41] It is suggested that this combination might be helpful in diagnosis suggesting the lymphoid nature of the testicular tumor. Involvement of the testes has also been rarely reported in acute leukemia and in Hodgkin's disease.

A peculiar feature of this case is the spontaneous remission which was noted without treatment, evidenced by regression of the glands after his first admission and by the transient nature of the facial nerve palsy.

A last feature to be recorded in this case is the terminal appearance of premature cells in the peripheral blood. These were most probably histiocytes. Histiocytic leukemia is a rare terminal event of reticulum cell sarcoma.[9]

The tumor did not respond to nitrogen mustard therapy but responded temporarily to deep x-ray therapy with the final fatal outcome.

CASE THREE

First admission: M. M.: a male aged 10 years, was admitted to the Children's Hospital on 25.5.1956. The main complaint was painless swelling of the left side of the neck. The condition started 4 months before admission in the hospital and progressively enlarged. Past history and family history were irrelevant.

Examination revealed a well nourished negro boy. The left upper deep cervical glands were enlarged together with the chain at the posterior border of the sternomastoid. The biggest (about the size of a walnut) was felt just behind the angle of the jaw. The glands were firm and not tender. There was some matting in the upper glands but no breaking down. The overlying skin was normal. The liver was 2 fingers enlarged and soft and the spleen was not palpable. No masses were felt in the abdomen. The rest of the physical examination was essentially negative.

INVESTIGATIONS

Tuberculin negative. Blood picture on admission Hb. 53%—R.B.Cs. 3,100,000—W.B.Cs. 4800—P. 62—L. 30—M. 4—E. 4.

X-ray chest and bones: negative.

A cervical gland was excised for biopsy: The microscopic examination of the lymph node revealed the absence of the lymphoid architecture and infiltration of the nodal tissue by a reticulum cell sarcoma. No giant cells or multinucleated cells were seen. (Fig. 11)

Progress: The child received deep x-ray therapy 3,000 r on the left side of the neck on 13.6.1956. The glands diminished markedly in size and he was discharged a month later in a good general condition with no glandular enlargement.

Second admission: We lost contact with the patient until 10.3.57 when he came to the outpatient and was readmitted. Parents stated that the neck glands started to enlarge one month after discharge from the hospital. On examination the cervical glands were excessively enlarged. Axillary glands on both sides were also moderately enlarged. The spleen was not palpable. He received another course of deep x-ray therapy followed by marked regression in the size of the glands. He was discharged on 9.6.57 with a fair general condition.

Comment: This is a fairly typical case of reticulum cell sarcoma, the primary site being in the neck glands. The commonest primary sites for R.C.S. are the retroperitoneal nodes, the gastrointestinal lymphoid tissue, particularly of the stomach and small bowel, the tonsils and the mediastinal lymph nodes. Lymphosarcomata of the head and neck are considered to have a more favorable prognosis[16]. The relatively long course of this case is in marked contrast with the rapidly fatal course of case 2.

SUMMARY

The classification of malignant lymphoma is reviewed on an embryological and anatomical basis. Malignant lymphoma excluding leukemia constitutes 10% of all causes of malignancy in infancy and childhood.

The follow up of 3 cases of malignant lymphoma in children is discussed; one case of giant follicular lymphoma in a boy 2½ years old and 2 cases of reticulum cell sarcoma in boys 9 and 10 years old.

The following features are to be noted:

(1) An intermittent course may be encountered in giant follicular lymphoma as well as in disseminated reticulum cell sarcoma.

(2) Exophthalmos which is not a rare feature of giant follicular lymphoma may be due to retroorbital deposits of tumor cells.

(3) Dissemination of reticulum cell sarcoma may occur all over the body. In the second case presented, tumor cells involved glands, liver, spleen, skull bones, facial nerve, skin and testis. Involvement of the testis by reticulum cell sarcoma is very rare but should be suspected in cases of bilateral malignant testicular swelling especially if associated with skin deposits.

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Generalized Vaccinia Successfully Treated With Lipoprotein-Nucleic Acid Complex (Reticulose)

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J.C. a 6½ month old female was first seen on February 5, 1958 with chief complaint of "blisters" over both buttocks, progressive over the preceding two days. She had been vaccinated against smallpox three weeks earlier, although an ammoniacal diaper rash had been present at that time. According to the history the primary reaction was severe; the upper arm bluish-red and swollen to the elbow. In addition there was a "rash which extended from the shoulder to the finger tips for four or five days" accompanied by a rectal temperature of 102-103°. Eight days after the primary reaction, a secondary pustular lesion appeared on the left buttock. On February 3, blisters appeared over both buttocks areas. The infant had been moderately fussy, but normally active. There had been no noted elevation of temperature. One brother, the father and grandfather had had asthma.

The infant was well-nourished, active, alert and responsive. There was no evident toxicity. The central nervous system was apparently normal. Rectal temperature was 99.4°. A large primary vaccination was present on the left arm. Widely scattered over both buttocks were multiple umbilicated purulent lesions, varying in size from small peas to the large serpiginous secondary lesion, measuring 1½ x ⅜ inch. Small umbilicated papules, 1-2 mm. in diameter were scattered over the scalp, forehead, chest and behind one ear. A few of these were purulent.

Because of the satisfactory therapeutic response[1,2,3,4] with Reticulose in the treatment of viral syndromes, it was decided to evaluate its effectiveness in this case.

Reticulose is a lipoprotein, nucleic acid compound. The mode of action of this preparation in combatting viral infection is not clearly understood, but in addition to its known non-specific effect in stimulating leucocytosis and phagocytosis, it may also have a

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direct action on the virus. This substance is free from sensitizing properties.

A stat dose of 1 c.c. of lipoprotein-nucleic acid complex (Reticulose) was given intramuscularly, to be followed by similar 1 c.c. doses at 10 p.m. and 10 a.m. The mother was instructed to keep the infant lying on her abdomen without a diaper. No local treatment was given.

The next examination was twenty-five hours after the first dose of Reticulose had been given. The improvement was dramatic. The large secondary lesion was dry and had started to fill in. The other buttocks lesions were collapsed and dry. The crust had already dropped from a'bout half of them, leaving healed bases. The small lesions on head and trunk were barely discernible. No new lesions were found. 1 c.c. of Reticulose was given intramuscularly at this time.

On the third day there was further filling in of the largest lesion. The others varied from small shallow depressions to fading erythematous macules. A cluster of five minute fresh papules was present on one buttock and a single new lesion was seen on the forehead. It was felt that the twenty-four hour interval between doses had been too long, so medication was changed to 1 c.c. b.i.d. Rectal temperature 100°.

Further regression of all lesions was noted on the fourth day. All scabs were off and the bases healed. No new lesions were found. Temperature 99.4°. The general condition was good. The infant was dismissed, with arrangements made for a single 1 c.c. dose of Reticulose to be given the following day, for a total of 8 c.c. Subsequent phone calls indicated there was no recurrence.

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Peterborough, N. H.

Intramuscular Iron in the Prophylaxis of Anemia in Premature Infants

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Oral iron medication has been used for many years in the prophylaxis of anemia in premature children. Colloidal suspensions of saccharated iron oxide have been available for intravenous use since 1947 (Nissim 1947), but the technical difficulties were too great for routine use in small children. The introduction in 1954 of an iron dextran complex, Imferon, for intramuscular use appeared to be a progressive step.

After intramuscular administration of Imferon slight toxic reactions such as headache, nausea, vomiting, chills, and fever (McLean Baird & Podmore 1954, Greenfield 1954, Jennison & Ellis 1954, Bourne 1955, Karlefors & Nordén 1958) were seen in about 20 per cent (Jennison & Ellis 1954, Karlefors & Nordén 1958), and local reactions, mainly staining of the skin, in 10-25 per cent (Dempster 1954, Nilsson & Söderhjelm 1956, Karlefors & Nordén 1958). A shock-like reaction has been described in a few cases both after intravenous administration of Imferon and saccharated iron oxide (Callender & Smith 1954, Granrud & Oster 1950).

In experiments on mice and rabbits, Martin et al. in 1955 showed that Imferon was absorbed from the site of injection in a few days. After injection of enormous doses of Imferon, only a few per cent was excreted in the first three days.

Using ^{59}Fe-labelled iron dextran, Nordén (1956) and Garby & Sjölin (1957) showed that in man one-half to two-thirds of the dose was absorbed from the site of injection in the course of 5-10 days, but that the rest was absorbed very slowly. About one third remained at the site of injection after 50-100 days. The activity in the plasma rose 4-6 hours after the injection and reached a

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peak after 24-48 hours. 5-10 days later no activity was found. In the red blood cells a trace of radioactivity was observed after 3-5 days, but the maximum activity was still not reached after 50-100 days. The first 20 days' urine was examined, but no radioactivity was found. This is in accordance with the observations made by McCance & Widdowson (1938) that even massive parenteral iron administration does not increase the iron excretion in the urine.

As the requirement of iron in normal children is about 200 mg during the first year of life (Coleman et al. 1955), and somewhat greater in premature infants it would seem possible to prevent the anemia usually seen in the 3rd-9th month of life by establishing a depot of iron by intramuscular injections of Imferon.

Good results of Imferon treatment are reported in adults and children (Cappell et al. 1954, Dempster et al. 1954, Jennison & Ellis 1954, Scott & Govan 1954, Grunberg & Blair 1955, Nilsson & Söderhjelm 1956, Wallerstein 1956, Karlefors & Nordén 1958).

In premature children, prophylactic treatment with Imferon intramuscularly has been reported by Gaisford & Jennison (1955). They treated 10 prematures in the third week of life with Imferon intramuscularly in doses from 150-250 mg. 10 other prematures acted as controls, receiving neither oral nor parenteral iron therapy. At first hemoglobin values decreased by the same amount in both groups, but after the 4th month of life the hemoglobin values were higher in the Imferon-treated group. In the 6th month the average hemoglobin values were 82 and 65 per cent respectively (100 per cent = 14.8 g hemoglobin/100 ml).

Hillborg & Nilsson treated 29 prematures with Imferon in the third week of life. The average dose was 150 mg iron. 28 prematures, who only received iron perorally in daily doses of 20-30 mg. bivalent iron (ferrosi pyrophosphas), acted as controls. They found the following hemoglobin per cents (100 per cent = 14.8 g hemoglobin/100 ml.) at the ages of

	3 months	6 months	8 months	12 months
Imferon group	78	83	83	83
Control group	72	77	77	79

MATERIAL AND RESULTS

In order to investigate the value of prophylactic intramuscular iron treatment combined with oral iron treatment in premature

infants, all prematures with uneven record numbers admitted in the period March 1957-February 1958 were treated with Imferon.

In prematures with a birth weight over 2.000 Gm. treatment was started soon after admission, but in children with a birth weight under 2.000 Gm. treatment was not started until they had reached 2.000 Gm.

The total dose of Imferon was in all instances 75 mg iron, given in three injections of 25 mg iron at intervals of two days.

The injections were given deep intramuscularly in the upper outer quadrant of the gluteal region. In order to prevent staining of the skin the following technique was used: Imferon was aspirated into the syringe with a thick needle. Before the injection a clean thin needle was fitted to the syringe. During the stab the skin was displaced. The injection was given slowly. During removal a slight aspiration movement was made in order to prevent deposits in the stab canal.

From the age of one month all prematures received oral iron medication, daily dose 250 mg ferro lactate. This oral treatment was continued until the last control.

During the admission the hemoglobin per cent was frequently controlled (100 per cent = 14.8 g hemoglobin/100 ml), and both the red blood cells and the reticulocytes counted. Examination of the blood was repeated at the control at the ages of 3, 6, and 9 months.

FIG. 1

Birth Weight in Gm	Total Material		No. of Prematures Examined at the Ages of					
	No. of Prematures Imferon		3 months Imferon		6 months Imferon		9 months Imferon	
	+	−	+	−	+	−	+	−
< 1,200	1	0	1	0	1	0	1	0
1,200–1,499	4	5	3	4	1	3	1	2
1,500–1,799	11	14	10	13	9	11	7	8
1,800–1,999	15	11	9	11	6	8	4	6
2,000–2,199	20	14	15	10	9	7	6	7
2,200–2,500	19	17	14	11	13	12	6	9
Total Number	70	61	52	49	39	41	27	32
Follow-up (in per cent)			77		61		45	

Fig. 1 shows the distribution of the total material set up in 6 weight groups, and the number of children followed up at 3, 6 and 9 months of age. Of 131 prematures 70 received Imferon. 77, 61 and 45 per cent were reexamined at the ages of 3, 6 and 9 months respectively. The numbers of Imferon-treated and non-treated controls were nearly equal; likewise the numbers of children in the weight groups from 1,500 to 2,500 Gm.

FIG. 2

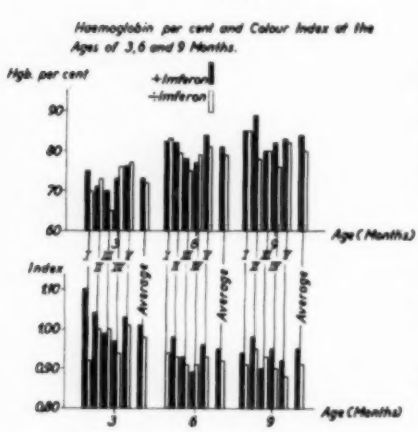

FIG. 3

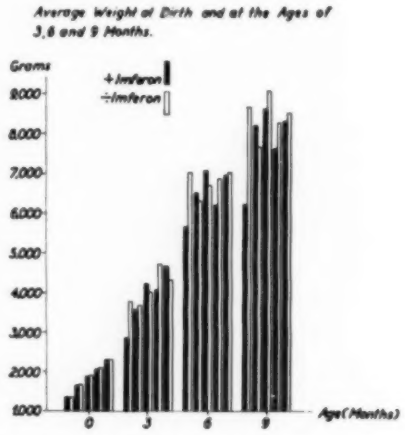

Fig. 2. Double-columns I-V represent every weight group from 1,200 to 2,500 Gm. Average represents all weight groups.

Fig. 3. The five double-columns represent every weight group from 1,200 to 2,500 g respectively.

Fig. 2 shows the average hemoglobin per cent above and color index below. The first five double-columns at each control check represent the weight groups from 1,200 to 2,500 Gm respectively. The black columns represent the Imferon-treated, the white the non-treated. The last double-column at every control check shows the average values for all weight groups. The hemoglobin values and index vary somewhat from group to group, sometimes higher in the Imferon-treated and sometimes higher in the non-treated groups. The average hemoglobin per cent and color index for all groups show higher values in the Imferon-treated than in the non-treated, at all control checks.

Fig. 3 shows the average birth weight and the average weight at the ages of 3, 6 and 9 months. The columns represent the

same weight groups as in fig. 2. Weight has increased most in the groups with smallest birth weight. The weight at 9 months differs only slightly in the weight groups from 1,500 to 2,500 gm. Throughout the study there were no significant differences in weight between Imferon-treated and non-treated.

In our series we saw neither general toxic reactions nor persisting local staining.

Increase in reticulocyte counts (over 2 per cent) were found in 25 out of 54 of the Imferon-treated, and in 15 out of 32 treated with iron orally.

DISCUSSION

In spite of prophylactic iron medication given both parenterally and orally, we did not succeed in preventing a slight anemia in the age from 3 to 9 months.

Despite the higher hemoglobin per cent and color index in the Imferon-treated group at all check points, no statistically significant difference was found between the values in the two groups.

At the age of 6 months, Gaisford & Jennison found an average hemoglobin per cent of 82 after Imferon treatment given as single therapy. At the ages of 6, 8 and 12 months, Hillborg & Nilsson found an average hemoglobin per cent of 83, 83 and 83 in the Imferon-treated group and 77, 77 and 79 in the group treated with iron perorally. At the ages of 6 and 9 months this was nearly the same as found in the present series after combined treatment with Imferon and iron given perorally (81 and 84 per cent) and treatment with iron given perorally only (79 and 80 per cent).

It may therefore be concluded that the effect of oral and parenteral iron treatment is the same and that a combined therapy with both oral and parenteral administration does not yield more than either of the two therapies alone. In cases where oral iron therapy is not practicable it seems reasonable to change to parenteral iron treatment, but in somewhat larger doses than used in the present series.

SUMMARY

Of 131 prematures, 70 were treated with Imferon intramuscularly (75 mg). In addition, all the prematures were treated with oral iron therapy (250 mg ferro lactate daily). Complications were not observed during or after treatment.

At the ages of 3, 6 and 9 months a slight anemia was found in both groups. No significant difference in hemoglobin values was found between the two groups.

Combined therapy with both oral and parenteral given iron therefore does not yield more than either of the two therapies alone.

In suitable cases it seems reasonable to replace prophylactic oral iron treatment with Imferon given intramuscularly.

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Clinico-Pathologic Conference

Memorial Hospital, New York
February 29, 1960

MARGARET S. LYMAN, M.D., Clinical Assistant Pediatrician
Presiding
HAROLD W. DAREGON, M.D., Chief, Pediatric Service
BENEDICT S. CATERINICCHIO, M.D., Assistant Resident, Pediatrics
RENATE DUCHESNEAU, M.D., Clinical Assistant Roentgenologist
LEE R. GARDNER, M.D., Assistant Resident, Pediatrics
ANNE BROUARD, M.D., Visiting Research Fellow, Pediatrics
PRAMOTE VIRANUVATTI, M.D., Chief Resident, Pediatrics
ROBERT JOEL, M.D., Resident, Department of Pathology

DR. CATERINICCHIO: *Present Illness*: This is a white male child, age 4 years, who was first admitted to Memorial Hospital on January 18, 1956, because of swelling of the left parotid region noted for 2 months prior to admission. Initially, the swelling had been considered to be mumps and it was treated conservatively for 3 weeks. It was then aspirated at another hospital but no pus or other material was obtained. He received a course of antibiotics with no decrease in the size of the mass.

Because of progressive enlargement, the patient was operated upon at another hospital for removal of the tumor. However, the mass was found to be too friable for excision and a biopsy was taken. "Benign fibroma" was the pathologic diagnosis on this specimen.

The mass had enlarged to such an extent that at the time of admission to Memorial Hospital, there was constant drooling from the left side of the mouth and constant tearing of the left eye. Past and family histories were noncontributory.

Physical findings showed the patient to be a well developed and well nourished child. There was an 8 x 8 cm firm mass in the left parotid and inframandibular area pushing into the left tonsillar area. The mass was moderately tender but not erythematous. A well-healed scar was noted at the posterior border of the left side of the jaw. The mass was noted to impinge to a considerable extent upon the oropharynx. There was no marked trismus. There were a few small nodes, rubbery in consistency and less than 1 cm in the left cervical area. No other adenopathy was present. The liver was thought by one examiner to be enlarged 2 cm below the right costal margin.

Laboratory findings: Hemoglobin, 16.3 gm/100 ml, leukocyte count 11,000/mm³ with 58% polymorphonuclears, 2% eosinophils, 6% monocytes and 34% lymphocytes; platelets were 86,000/mm³; a count three months later was 296,000/mm³. A bone marrow aspiration was normal. No extrinsic cells were seen. Urinalysis was normal. Total protein was 8.7 gm/100 ml, albumin 6.4 gm/100 ml; uric acid 4.6, blood urea nitrogen 16.5, calcium 14.5 and phophorus 5.6 mg/100 ml; alkaline phosphatase 8.3 units. Hemoglobin 5 days after admission was 15 gm/100 ml. Leukocyte count was 6,000/mm³.

The biopsy specimen submitted by the other hospital was reviewed and a diagnosis of malignancy was established.

Roentgenologic studies of the following areas were obtained during the patient's illness: skeletal survey including skull, entire spine, pelvis, both humeri and femori, chest, mastoids, neck, orbits and left mandible.

Therapy and Course: Radiation therapy was given to the left parotid area from January 19, 1956 to February 27, 1956, with a total tumor dose of 3,300 r. Ten radon seeds were implanted on January 20, 1956. There was rapid regression of the tumor, such that by February 9th, the mass measured 3 x 2 cm and by February 23, there was no evidence of disease. A moderately intense skin reaction was noted in the region of the left parotid area.

The patient remained well until April 2, 1956, when he began to experience nausea and vomiting. He was admitted for the second time on April 10, 1956, because of these symptoms plus occasional headaches and dizziness on standing. There had been no fever, bleeding, abdominal pain, convulsions or fainting.

Physical Findings: At the time of the second admission, there was facial asymmetry and fullness of the left eye and a dilated left pupil which reacted to light. There was no lateral movement of the left eyeball. Fundi were normal in both eyes. There was a peripheral left facial paralysis including the forehead, eyelids and lower face. The uvula was pushed to the right side by a mass extending from the soft palate. There was impaired sensation over the distribution of the left trigeminal nerve. A diffuse firm swelling of the left postero-lateral buccal area, including the hard palate and tonsillar area was noted. Hearing was normal; neck and tongue motility were normal. The remainder of the examination was not remarkable.

Therapy and Course: X-ray therapy was given to the skull in

the region of the sella turcica and left zygomatic area from April 12 to April 21, with 1,600 r total tumor dose.

On April 17, the patient was noted to have brief twitchings of the right side of the face and later the same day of the left hand and left leg with brief spasticity noted. Barbiturates were administered for 3 days with apparent control of the seizures. On April 22, the patient was noted to be "either asleep or semi-comatose". At moments he could be easily aroused and was rational. At other moments there was no response to deep pain. On April 23, he stated during one of his lucid moments that he could no longer see. The left pupil was fixed, the left eyelid drooped and did not open. Papilledema, 1+, was noted on the left.

On April 24, right facial paralysis was noted as well as a loss of sensation in the right cheek and poor hearing in the right ear. Positive Brudzinski and Koenig signs were present. Deep tendon reflexes were absent. There was no Babinski sign, no clonus or fever. Difficulty swallowing, irregular respirations, incontinence and rales developed during the next 4 days and the patient expired on April 28, 1956. On the day of death, blood pressure was noted to be 170/120. During the last 2 weeks of illness, the patient required almost continuous intravenous administration of fluids. Throughout this period, the blood chemistries remained within normal limits.

DR. DARGEON: Shall we proceed with the possibilities and the whys?

DR. CATERINICCHIO: The case is that of a 4-year-old boy who presented with a mass in the parotid region which presumably was of neoplastic origin and from the course of the disease—the course being 6 months from the onset of first symptoms—it appeared to be a rapidly progressive lesion, and from the course alone, it could be said to be malignant. The presence of a mass in the region of the parotid in this age group I suppose would have to be considered either as a primary tumor or a metastatic node.

First of all, reviewing his chart and his course, there isn't much in this, per se, that can help us. The laboratory findings as listed on the first admission were all within normal limits except for the calcium which was elevated. It was 14.5 mg/100 mls; also a platelet count which on admission was 86,000 mm^3. I would like to know if these were persistent findings, whether he had a persistent hypercalcemia, and whether the platelet count was truly this low. I would like to defer a review of the x-ray findings for a moment and discuss what I think are the possibilities of a metastatic lesion

in this area, in the left parotid and inframandibular area. The one that seems most likely or the only one that I think is most likely would be a metastatic focus, secondary to a neuroblastoma, the primary being in some area, possibly the abdomen. However, the mass itself behaved in such a malignant fashion that I would presume it was primary in this area and we could probably discount a metastatic lesion, although we will have to see the x-rays to discount that fully.

Of the primary lesions in this area, shall I list them?

I think we would have to consider first of all in the inframandibular area a lymphoma. I am not mentioning nor listing these in order of likelihood. Secondly, we would possibly have to consider a thyroid cancer with this being a node metastatic from the thyroid; also in this area, we would have to consider osteogenic tumors, possibly a neoplasm of the bone which would be the mandible, so we could list osteogenic sarcoma, and possibly Ewing's tumor.

To be considered also are tumors of the salivary glands, of the parotid and submaxillary salivary glands, and this particularly involves a tumor of the parotid. Too, we would have to consider sarcoma of the soft tissues in this area, fibrosarcoma and liposarcoma, but particularly rhabdomyosarcoma. Then there are other rarer lesions which can appear in this area such as chordoma and angiosarcoma, and others which are rarer still.

I think lymphoma can be discounted on the basis of the original report of the biopsy. This is in retrospect, but I think it could probably have been picked up on the first biopsy; also it is a rapid course for a lymphoma. With lymphoma, I suppose we should consider Hodgkin's disease here too; I believe the course in this case is much too rapid and I don't believe this child is in the expected age group. The same considerations would apply to thyroid carcinoma. I think it would be first of all unusual in a child of this age, and secondly the course of his illness was much too rapid for a thyroid carcinoma. Osteogenic and Ewing's sarcoma I think can be discounted because of the location of this mass, and also because of the rather rapid course.

The tumors of the salivary glands I suppose are a possibility in this child, although mixed tumors of the parotid gland are rare in children; however, the course of the illness and direct extension into the oral pharynx and the difficulty the child had with facial paralysis might make this a possibility. Rhabdomyosarcoma I think would probably be the most likely diagnosis in this child because of the rapid course; the fact that this tumor was presum-

ably quite anaplastic was suggested by its radiosensitivity initially. After the patient received his first course of radiation, there was rapid regression. I think his symptoms at the final illness were due to direct extension along the course of the facial nerve, with paralysis of the trigeminal, and also possibly direct extension into the cranial vault through the base of the skull. Therefore, I think the most likely diagnosis is rhabdomyosarcoma, and I believe this caused his demise by direct extension into the cranial vault. Possibly there were distant metastases into the brain causing increased intracranial pressure and also respiratory paralysis. I would presume that his death was due to respiratory paralysis.

I would like to see the films of the mandible and upper neck and also the skeletal survey, and I would just like to ask whether or not there was any mass ever palpable in the abdomen other than a questionably enlarged liver.

DR. LYMAN: There were no masses ever palpated in the abdomen and the liver at the time of the second admission was not thought to be enlarged.

DR. DUCHESNEAU: These are all films taken toward the end of the course and the most striking findings may be seen in the frontal views of the skull. The areas of soft tissue mass may be seen displacing the mandible laterally and inferiorly causing some thinning or pressure erosion primarily on the condylar portion which seems to be displaced.

This is a view of the opposite side which seems to be in a relatively normal position. There is no evidence of erosion in the temporal bone. All this would suggest that there was a tumor or mass below the condylar fossa. In the view of the facial bones, the orbit itself seems to be intact.

The zygoma is pushed up a little and also looks a little thin. I believe there is some erosion here on the body of the zygomatic bone, the lateral part of the maxilla, thus pushing the mandible out and down and the zygomatic arch upward. The main part of the mass at this time seems to be on the inside, or the frontal side of the mandible. In a film of the base of the skull, (this is unfortunately not a stereo view), we see an abnormal soft tissue mass medially overlying the pharynx. The foramen ovali may be seen here. On the abnormal side, there is absolutely no bone structure left. We can see the mass also extending upward and eroding the face and skull on that side. The palate cannot be seen so well without a stereo film. There may be a little soft tissue swelling on the outside of the cheek.

DR. CATERINICCHIO: I think the roentgenologic findings certainly are compatible with a tumor of the soft tissues causing erosion by pressure and producing most of its effects by direct extension. I think now the diagnosis is narrowed to one of the soft tissue tumors and of these I believe that rhabdomyosarcoma is the most malignant in nature, and would be compatible with a lesion which showed such rapid progression. To the possibilities that were mentioned, I don't think any more can be added. My understanding is that the group of tumors described as tumors of the nasopharynx would include any soft tissue tumor in this area.

DR. LYMAN: It is regrettable that a neurologist was unable to be present. I would like to ask the group for their opinions. Dr. Caterinicchio has suggested a rhabdomyosarcoma as the most likely diagnosis. Dr. Patuleia, would you like to begin by telling us what you think this patient's lesion is?

DR. PATULEIA: I believe it is a soft tissue tumor primarily eroding the bony structures, a myosarcoma. It appears to be substantiated by the x-ray findings.

DR. LYMAN: What would you think the cause of death might have been?

DR. TENSUAN: The most likely cause is an intracranial extension of the soft tissue mass. At the terminal point of his illness, he had all sorts of neurologic symptoms: facial paralysis and Brudzinski and Koenig signs which point to intracranial involvement. He also had difficulty swallowing, and vomiting just prior to death. Convulsions were also noted which would point to intracranial involvement.

DR. LYMAN: What specifically do you mean by intracranial involvement. Do you mean pressure phenomenon or invasion of a vital center in the brain?

DR. TENSUAN: I think pressure may have been the cause of his not being able to see at one time, and the lethargy or semi-coma. If this were some kind of cerebrovascular accident—any tumor could erode through the walls of a large blood vessel, causing hemorrhage—it might have given a different kind of picture of neurologic changes, and it might have been more gradual.

DR. LYMAN: Do you think there may have been a cerebellar cone causing his acute demise, resulting from increased intracranial pressure?

DR. TENSUAN: I don't think it was an acute demise; the symptoms of irregular respirations, incontinence and rales were noted several days prior to death, and he later became semi-comatose.

DR. LYMAN: Am I correct in interpreting your statements to mean that this boy's primary problem during his second admission was one of increased intracranial pressure?

DR. TENSUAN: Yes.

DR. LYMAN: Dr. Viranuvatti, would you care to give us your opinion as to the cause of death?

DR. VIRANUVATTI: I agree with your interpretation.

DR. LYMAN: You think rhabdomyosarcoma is the most likely diagnosis?

DR. GARDNER: I think I'd go along with rhabdomyosarcoma and, in addition, infiltration and pressure with some herniation of the brain stem as the immediate cause of death.

DR. LYMAN: You think pressure was caused by the lesion?

DR. GARDNER: I think pressure with necrosis and herniation.

DR. BROUARD: I think it was a parotid tumor.

DR. LYMAN: What kind of a parotid tumor?

DR. BROUARD: A mixed parotid tumor. His final neurologic symptoms could either be pressure on the brain stem or an extension or metastasis from the original tumor into the brain stem.

DR. DARGEON: Well, I agree. I think it is a primary tumor in the head whether originally in the parotid, nasopharynx, or from the base of the skull. The first signs we had were those of the excessive growth into a less resistant zone such as the nasopharynx and the intracranial cavity. I don't see that we can entirely rule out metastatic tumor, but we certainly don't have any support. I would say that before we had x-ray signs, I would lean initially toward the parotid tumor, a mixed tumor being the most common, and next the lymphoma, next to that rhabdomyosarcoma, or one of the tumors of a malignant nature that occur from many sites of origin and many other soft parts of the body, such as angiosarcomas, angiopericytomas. There is also a synovial sarcoma which arises around bones and joints, which is a possibility. However, at the age of the child, of course, and the position of the tumor, one of the most common tumors in the nasopharynx in the young is the angiofibroma but this is not seen in most children at this age—4 years. Angiofibroma is chiefly a tumor of pre-adolescence, or the adolescent.

Then too, we have some assistance here in the radio-sensitivity of the tumor. This could possibly be a rhabdomyosarcoma. I would be more inclined to think of a more sensitive tumor, so my first impression would be that it is a lymphoma of some sort. I think rhabdomyosarcoma would be second, synovioma third, and

an intracranial lesion connected with angioma might be another consideration. I think death was due to extension, possibly so much as may cause invasion, vascular difficulty in the brain itself. I don't find the results of a lumbar tap.

DR LYMAN: No lumbar puncture was done.

DR. GARDNER: I don't see why the original diagnosis could not also be accepted—a benign fibroma, but the type of fibroma which actually becomes fibrosarcoma

DR. LYMAN: It is unfortunate but only one biopsy was taken. It was read elsewhere as a fibroma. May we have the pathologist's report, unless there is further comment or discussion?

DR. JOEL: I would like to review briefly the important findings at necropsy and then we will discuss this type of tumor more fully. First of all, the only positive findings in the necropsy were relative to the face, head, and thorax. The lungs weighed 160 gm, right; 150 gm for the left and the only finding in the lungs was an acute bronchopneumonia and some intra-alveolar hemorrhage. The rest of the organs of the abdomen and thorax were not significant, either grossly or microscopically. The liver which was not palpated toward the end of the clinical course weighed 600 gm and showed nothing of interest. Now the main findings in this case were located as we opened the skull. We found a large tumor mass which was involving the greater wing of the sphenoid and the petrous portion of the temporal bone. This mass also extended into the pons intermedia and the pituitary gland microscopically. It had gone into the left portion of the pons, the cerebellar peduncle, the dentate nucleus, the occipital lobe, and the left motor cortex. Of course, a mass was found in the original parotid area. The tumor in the brain was apparently an extension upward from the mass located in the parotid region.

Perhaps we can clarify some of the problems on the original biopsy. I will try to show you two slides: 1) the original biopsy which was read elsewhere as a fibroma, which we read here as a malignant tumor; and 2) a classic picture of this tumor as it was located in the region of the pons.

First of all, this is the original biopsy that this child had, and you will note that even at low power magnification, this is a rather cellular lesion. The tumor is quite cellular and there are portions where the cells are quite spindly and quite dark. The tumor is characteristic of embryonal rhabdomyosarcoma. We have recently reviewed thirty-seven cases of this type of tumor and several of the following facts have been of particular interest: The predominant

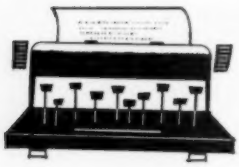
cell of this neoplasm is a single cell with elongated nucleus. The cytoplasm is usually quite red and you may or may not see striation. The age of the patient in our cases ranges from seven weeks up to twelve years.

The anatomic sites of this tumor in the present series are as follows: Eight from the orbital cavity; seven from the soft tissues of the neck; six from the nasopharynx; five from the cheek; three from the mandible; three from the palate; two from the tonsils; one from the gingiva; one from the parotid and one from the external auditory canal. Of the patients that we've seen here almost in all cases, the presence of the tumor itself was the initial symptom. The presence of a bulging mass prompted the patient to see the doctor. The median survival time of the patients from the initial discovery of the tumor to death was ten months. Of the total patients seen, return of the tumor after the first treatment was usually within two weeks to twenty-four months. Metastases from this tumor occurred quite rapidly. The usual time interval noted for recurrence was under three months.

The treatment of these tumors, because of their location, is usually radio-therapy. It is extremely difficult to treat a tumor like this by surgery because most of them occur around the head and neck.

The original interpretation of the biopsy material on this particular patient, as you can see by the slides we've shown, is extremely diffcult. The fact that it was called a fibroma is not at all surprising; in the original material obtained at biopsy in these patients a number of diagnoses other than sarcoma was made.

In summary, we have a tumor which began in the parotid region of this 4-year-old child which spread to involve the head and neck and ultimately involved the brain. The pathology in the brain was quite extensive and explained many of the localizing neurologic signs this patient had. As far as the present case is concerned, we have a 4-year-old male who developed a tumor diagnosed as a fibroma some six months prior to death. On a review of the material this was an embryonal rhabdomyosarcoma of the region of the parotid gland.



Books . . .

Authors' Summaries . . .

Edited by

MICHAEL A. BRESCIA, M.D.

THE CHILD WITH MONGOLISM (Congenital Acromicria) by Clemens E. Benda, M.D. Cloth. Pp. 276. Illustrated. Grune & Stratton, New York and London 1960. $9.50.

The author has written an excellent monograph on mongolism and the book is highly recommended particularly to pediatricians and obstetricians. The book covers the subject completely and the chapters dealing with the diagnosis of mongolism at birth and anatomic and X-ray observations have great clinical value. The author is well versed in the subject and demonstrates a genuine compassion for the mongoloid child as well as for the parents. The author is fairly optimistic within certain limitations and he tries to dispel the pessimism that seems to enshroud the attending physicians as well as the family constellation on the appearance of a mongoloid child. Although there is no specific treatment for the condition, nevertheless in the chapter on the principles of treatment the author outlines some of the procedures that definitely help to improve the status of the mongoloid child.

At the end of the book there is appended an extensive bibliography as well as a recommended reading list for parents, social workers, educators and psychology students.

The authors have some questions and answers regarding mongolism and cerebral palsy. This reviewer wonders if it would not have been of value to have included some questions and answers regarding mental retardation in general and specifically some of the metabolic disorders such as phenylketonuria. These can be included in future editions.

The book is recommended to mothers and a cheaper paper back edition might very well give it widespread distribution. Some pediatricians might even give them as a gift to some of the more "question asking" mothers. M. A. B.

ADVANCES IN PEDIATRICS, Volume XI. The Yearbook Publishers, Inc., Chicago, Ill. 1960. $11.00.

This latest volume in an excellent series maintains the high standards set by previous editions, with six monographs of diverse appeal.

C. D. Cook and his colleagues in Boston have reviewed the progress which has been made in what is probably the major pediatric problem of the day, respiratory difficulties in the newborn. In spite of 156 references, he reiterates that little appreciation of mechanisms of disease is possible, scant knowledge of the fundamental development of the respiratory system is at hand, and much more work must be done.

Cooke and Ottenheimer with many more references review a much narrower subject, the central nervous system control of sodium concentration on the brain. This article is a must for all pediatricians who treat disorders of salt and water metabolism—and what pediatrician does not?

Deamer has reviewed the chronic conditions which are seen more frequently by pediatricians than any other, namely, allergy in childhood. This monograph is out of place in a book which emphasizes "advances" but is a clearly written monograph reviewing currently practiced concepts in the diagnosis and management.

Meneghello's article on infantile diarrhea in Chile is an interesting report of attempts to manage a chronic environmental problem secondary to poor sanitation, poor hygiene habits, and low cultural, economic, and educational levels.

For those who know nothing about aminoaciduria and amino acid metabolism, Snyderman and Holt's article is a good one to start with. Since 34 conditions are referred to in as many pages, the treament is necessarily superficial, but is a good introduction to 146 references.

Finally, May G. Wilson's article is a summary of her experience with hormone therapy in Rheumatic Fever. It must be pointed out that her experience is not shared by many rheumatologists, which explains why the treatment of active rheumatic carditis remains controversial. J. Frederick Eagle, Jr., M.D.

Ward B. and Hunter, W. M.: THE ABSENT TESTICLE. (British Medical Journal 5179:1110 April 9, 1960).

A survey of 19,024 boys at the ages of 5, 8, 11, and 14-17 years was made in 1957 and 1958 to determine the number of unilateral and bilateral undescended testicles.

A marked fall in the percentage of these conditions was found to occur between 11 years and 14-17 years.

It is suggested that hitherto undescended testicles may naturally descend into the scrotum at puberty. If this is true it may produce a reorientation in the approach to treatment.

Chapman, A. H.: EARLY INFANTILE AUTISM. (A. M. A. Journal of Diseases of Children 99:783 June, 1960).

Early infantile autism is a disorder beginning in infancy and characterized by withdrawal from interpersonal relationships, obsessive need to maintain the sameness of the physical environment, preoccupation with things as opposed to people, and various disturbances of language. The prognosis is guarded, particularly in those children who do not learn to speak by the age of 5. The value of treatment in altering the course of this disorder is not proved. It is important that this syndrome be recognized so that these children can be appropriately managed rather than erroneously consigned to the categories of the mentally deficient, the deaf-mute, or the organically brain-damaged.

A COMPARISON OF THE EFFECT OF PREDNISONE AND ACETYLSALICYLIC ACID ON THE INCIDENCE OF RESIDUAL RHEUMATIC HEART DISEASE. Combined Rheumatic Fever Study Group. (The New England Journal of Medicine 262:895 May 5, 1960).

In a carefully controlled co-operative study of 57 patients in their first attack of unequivocal rheumatic carditis treated within twenty-eight days of onset, large doses of prednisone given for twelve weeks were not found to be superior to acetylsalicylic acid in preventing residual rheumatic heart disease. The chief action of both prednisone and salicylates appears to be to suppress the inflammatory reaction caused by this disease. In many patients, however, even if the acute symptoms are promptly and well controlled, cardiac damage is not prevented.

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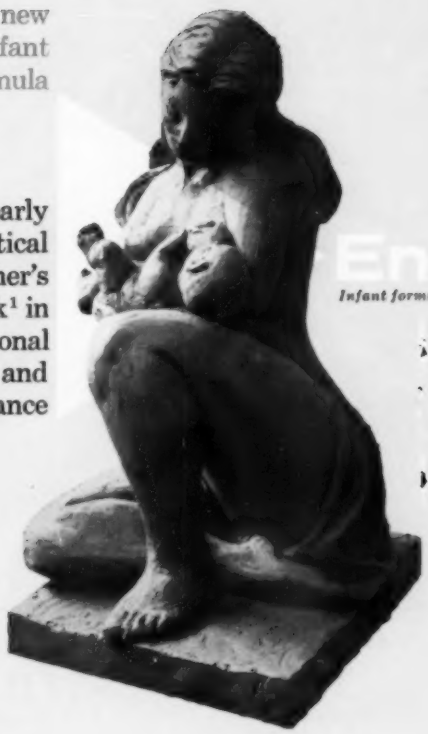

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1. Macy, I. G.; Kelly, H. J., and Sloan, R. E.: With the Consultation of the Committee on Maternal and Child Feeding of the Food and Nutrition Board, National Research Council: The Composition of Milks, Publication 254, National Academy of Sciences and National Research Council, Revised 1953. 2. Brown, G. W.; Tuholski, J. M.; Sauer, L. W.; Minsk, L. D., and Rosenstern, I.: Evaluation of Prepared Milks in Infant Nutrition; Use of the Latin Square Technique, J. Pediat. 56:391 (Mar.) 1960.

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